

Protherics PLC Annual Report 2002

protherics

In 2001, the pharmaceutical industry has been a year of significant change. The industry has seen a number of major mergers and acquisitions, and the regulatory environment has become increasingly complex. Despite these challenges, the industry has made significant progress in the development of new drugs and the improvement of existing ones.

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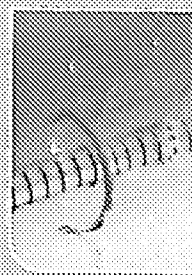
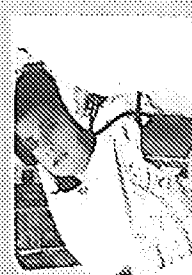
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Product	Principal uses	Status	Licensed/holder	Key milestones
<b>PRODUCTS LAUNCHED</b>				
<b>GlaxoSmithKline</b>	Rhizomale	Approved by FDA October 2000. Launched 01 January 2001	Alkermes (USA)	Phase 1/2/3
<b>GlaxoSmithKline</b>	Current advice	In market at various patient cases	Swedish Institute of Technology	Phase 1/2/3
<b>GlaxoSmithKline</b>	Recovery of organ toxicity	Approved by FDA August 2001. Launched Feb 2002	Relaxin (USA)	Phase 1/2/3

<b>PRODUCTS IN CLINICAL TRIALS</b>				
<b>GlaxoSmithKline</b>	Hypertension	Phase 1	Relaxin (USA)	Phase 1/2/3
<b>GlaxoSmithKline</b>	Pediatric license	Phase 1/2	Relaxin (USA)	Phase 1/2/3
<b>GlaxoSmithKline</b>	Treatment of organ toxicity	Phase 1/2	Relaxin (USA)	Phase 1/2/3

<b>PRODUCTS IN RESEARCH</b>				
<b>GlaxoSmithKline</b>	Cancer therapy	Research/clinical of principle	Relaxin (USA)	Phase 1/2/3
<b>GlaxoSmithKline</b>	Kidney failure	Research	Relaxin (USA)	Phase 1/2/3

<b>OTHER PRODUCTS</b>				
<b>GlaxoSmithKline</b>	Development of BSC in children	Launched	Relaxin (USA)	Phase 1/2/3
<b>GlaxoSmithKline</b>	Animal corneal transplantation	Phase 1/2	Relaxin (USA)	Phase 1/2/3
<b>GlaxoSmithKline</b>	Refinement of BSC in children	Application for approval in UK submitted in 2001	Relaxin (USA)	Phase 1/2/3

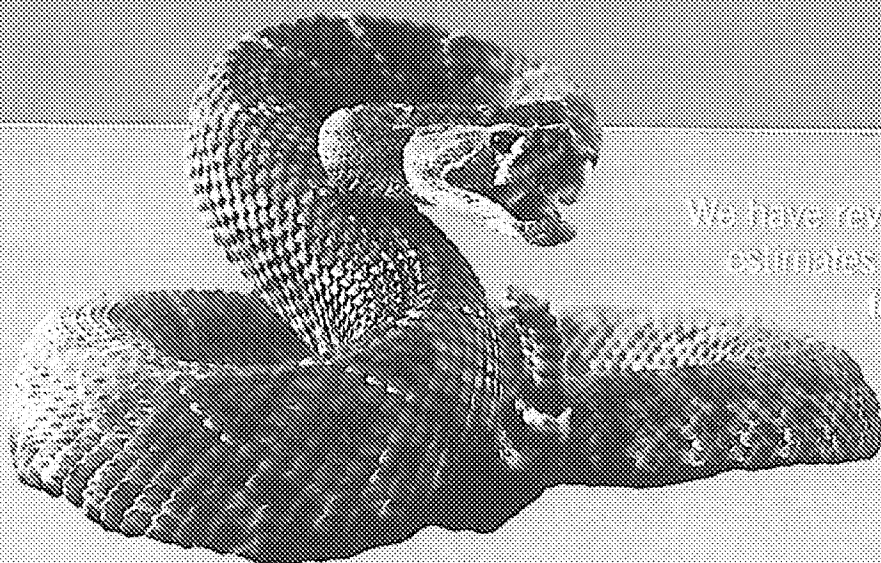
## Chief executive officer's review

This past year has seen the beginning of a fundamental change in the relationship between the major pharmaceutical companies and their young biotechnology brethren. In recent months 5 of the larger pharmaceutical companies have announced profit warnings, and it is clear that the historic growth rates of 15-20% per annum will be no longer achievable – for many growth may be less than 10% per annum. These lowered growth rates mirror the increasing cost of drug development for big pharma, with lengthening approval times and fewer new drugs coming to market. In contrast, more and more new drugs are being developed by biotechnology companies, typically at lower cost. On average, it costs only half as much for a biotechnology company to reach an NDA approval as big pharma. Furthermore, more targeted biotechnology-derived treatments are splintering what used to be single block-buster markets into smaller fractions. Five biotechnology-derived drugs have achieved sales exceeding \$1 billion. As biotechnology companies become more commercially focused, more of them will seek to market their own products and the number of mid-sized biotechnology companies is likely to grow. As biotechnology-derived products reach the market, there is likely to be a shift in the relative capitalisation of biotech vs pharma. This change is already happening, most notably in the US. Nonetheless, we believe biotechnology remains significantly undervalued compared to the established pharma sector.

Prothenics is well placed to take advantage of these changing dynamics. Today, in an environment where the balance sheet takes centre stage, we are fortunate to be able to fund our own early stage clinical development. In the US, we have a team with experience from the hands-on management of 15 trials involving 466 patients at more than 100 trial sites. Between October 2000 and December 2001, only 26 drugs were approved by the FDA. Two of these approvals were achieved by Prothenics. With the approval of DigiFab™ in the past year, we now have two products marketed in the US. Consequently, we have been able to develop a more commercial perspective. Now, our challenge is to become consistently profitable.

### Operations

This past year has seen larger orders for CroFab™ and DigiFab™ than we initially projected. We have worked hard to expand our capabilities in Australia and Wales to meet this demand. In Australia, productivity has improved dramatically in the processing of serum, and last year almost 20 tons of serum were produced. In Wales, our batch sizes of CroFab™ have more than doubled and we have halved the time to completion from 8 to 4 weeks. Further improvements are anticipated in the current year. The appropriate capital expenditure is now being made to increase batch sizes and reduce cost of goods further.



We have revised upwards our estimates of the market opportunity for CroFab™ to \$75 million per annum.

William Diamondback Rattisave  
(CroFab™ Agent)

## Chief executive officer's review *(continued)*

Careful attention is being paid to risk management, including dual sourcing of venins, geographical separation of sheep flocks, and filling and freeze-drying.

Looking forward 12 to 18 months, we plan to expand CroFab™ production capacity, allowing us to build adequate inventory and meet the demands of a growing and seasonal market.

As our need for clinical trial quantities of vaccines expands, we find it an advantage to be in direct control of our own FDA and MCA approved manufacturing facility. Manufacturing is often a bottleneck for small companies, who find it difficult to locate a supplier of smaller quantities of drugs for clinical trials. This past year we have successfully transferred the manufacture of our angiotensin vaccine from external contractors. This product is now made at our facility in Wales, at a considerable cost saving.

### Portfolio Review - Marketed products

#### CroFab™

CroFab™ has been very well received by physicians who manage snake envenomations. After a full year in the marketplace, it presents a new standard of care, with an excellent safety profile, even in large doses. Physician demand suggests it will continue to be used earlier, more often, and in milder bites than the previous treatment. We have revised upwards our estimation of the potential size of the market opportunity to \$75 million, as CroFab™ use expands into milder pit viper bites, such as those caused by Copperheads. While the majority of rattlesnake bites occur

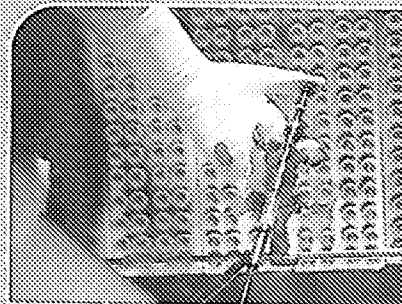
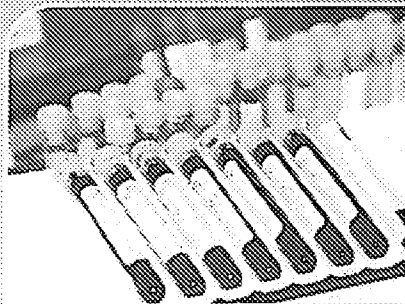
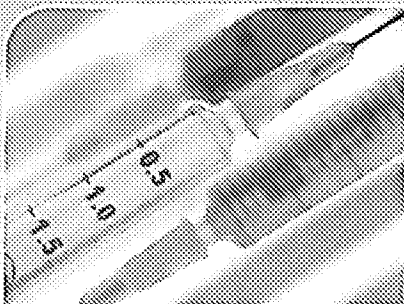
in the Western US, Copperheads are found mostly in the Eastern US. Although seldom fatal, these bites can be serious, with victims often incapacitated for several months. Copperheads account for nearly 40% of pit viper snake bites (including rattlesnakes) in the US. We expect to see a growing number of Copperhead bites treated with CroFab™ as production volumes increase further over the next 12 to 18 months.

#### DigiFab™

DigiFab™ enters a niche market in the US. With only one other competitor in this \$20 million market, we believe that DigiFab™ will make a significant contribution to our revenues in this next financial year. We hope to extend our marketing capability into Canada, where we will market DigiFab™ ourselves, and we are planning an application to the Canadian regulatory authority this year. Bulk sales to Sri Lanka, where the product is used for the management of Oleander poisoning, should provide further modest revenues.

#### ViperaTab®

ViperaTab® has had an excellent year, with sales of approximately £350,000 as hospitals have built inventory in what has been a year with an exceptionally large number of bites. Although ViperaTab® will remain a small product, its contribution is significant as margins are good. A very high penetration has been achieved in the Scandinavian market, and future growth is planned by expansion into other European countries.





## Chief executive officer's review (continued)

### GrR (Phlog<sup>TM</sup>)

This vaccine, developed for the management of prostate cancer, is licensed to M.L. Laboratories plc (M<sup>L</sup>). We are reviewing with M<sup>L</sup> the possibility of using recent improvements in our vaccine technology to test a more potent vaccine in this indication.

### BSE Test

BSE or "mad cow disease" has become a global problem. Reported cases this year in Japan confirm that the market for BSE tests now extends beyond Europe. Our revenues in the financial year just ended (£1.4 million) come mostly from our licensee, Enler Scientific Limited's sales in Ireland. Enler's agreement with Abbott, extending sales into Europe, provides an opportunity for continued growth of the revenue stream. We have retained our intellectual property rights for the testing of prions (such as Creutzfeldt-Jakob Disease) in man.

### Pratherics Tomorrow

Our successes these past two years, with two FDA approvals, a growing revenue stream, and a business now approaching self-sufficiency, is encouraging. Our staff has matured -- growing from a research and development team completely dependent on external funding, to an integrated team that recognizes that their efforts pay for our own research and development. Our financial wellbeing remains dependent on continued reductions in cost of goods, and we are making every effort to improve our manufacturing

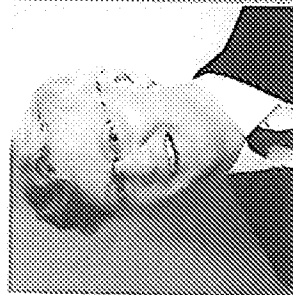
process. We have two clinical programmes addressing major diseases, now in Phase II-IIb, backed up by promising preclinical projects. We have a talented, experienced team that can and wants to do more.

These recent months have not been kind to smaller biotechnology companies, particularly in the UK, and we are no exception. However, with a stronger balance sheet and our own revenue stream, macro changes in the dynamics between big pharma and smaller biotech should work in our favour.

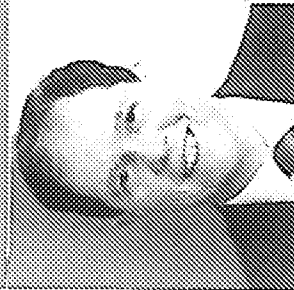
At Pratherics, we feel we must do more to ensure that our achievements are recognised, for the benefit of all who have supported us. Moving into the next financial year we are closing in on our immediate goal: financial independence in combination with a vibrant, and valued, development pipeline.

*Andrew J Heath*

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Chief Executive Officer



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